

Effects of chronic beta-blockade on intra-arterial blood pressure during motor car driving

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SUMMARY Continuous intra-arterial blood pressure recordings during motor car driving were performed in 15 patients with untreated essential hypertension, using the "Oxford" recording technique. Each subject was an experienced driver who used his car every day, and for the study drove from his work place to the hospital during the later afternoon. This drive took place in urban traffic and the average duration was 20.9 minutes. Blood pressure during car driving was remarkably stable, and the average systolic and diastolic pressures were similar to the mean daytime pressure. After 16 weeks of treatment with oxprenolol each patient was restudied. Blood pressure during driving had dropped from 176/107 to 160/93 mmHg, but the blood pressure response to driving and blood pressure variation during driving (expressed as the coefficient of variation) were unchanged. After treatment, the mean daytime systolic pressure was lower than the mean pressure during driving, but the relative antihypertensive effect during driving was similar to that observed in the same patients during dynamic exercise on a bicycle ergometer. No drug-induced side effects occurred and there were no apparent effects on driving ability. Chronic treatment with oxprenolol reduced blood pressure during car driving without affecting the normal blood pressure response to driving.

The efficacy of antihypertensive drugs is usually assessed by measuring the blood pressure of patients indirectly, using a sphygmomanometer, when they attend the hospital clinic or the doctor's surgery. Though this is a simple non-invasive method of assessing an individual patient's blood pressure, it samples only a small amount of data from a subject at rest and gives no information on the antihypertensive effects of a drug outside the controlled hospital environment.

The development of a method for recording accurately intra-arterial blood pressure on magnetic tape¹ in patients who are free to return to their own work during the day and to their own home at night has made it feasible to undertake more detailed studies. With very few exceptions the patients are completely free to return to their normal daily activities. This technique has been used to assess the effect of antihypertensive drugs outside hospital by making paired observations in groups of patients before and during chronic treatment.^{2,3} By means of a diary sheet detailed correlation of their activities during a recording may also be obtained.

Motor car driving is an activity performed by a large percentage of the adult population. There is some evidence to suggest that driving is a "stressful" activity,^{4,5} though intra-arterial blood pressure changes during driving may be small.⁶ There has previously been no attempt, however, to investigate the effects of drug treatment on blood pressure in hypertensive patients while driving a motor vehicle.

The purpose of this study was to examine the effects of chronic antihypertensive treatment with a beta-adrenergic blocking drug on blood pressure in subjects driving their own motor vehicle in the London area. The antihypertensive effect was compared with that observed during graded exercise on a bicycle ergometer, because of the difficulty of standardising or characterising the effect of driving in traffic on the public highway. In addition, data were available in each case on the response to treatment assessed by clinic blood pressures and mean daytime ambulatory pressures.

Patients and methods

Fifteen consecutive patients who had been referred to the Harrow Hypertension Clinic and who

normally drove a motor car to and from their place of work were investigated. They were all men and their mean age was $48.6 (\pm 10.6)$ years (standard deviation). In each case hypertension was confirmed by the presence of a clinic diastolic pressure in excess of 95 mmHg on three occasions (the mean clinic blood pressure for the group was $174 \pm 22/113 \pm 17$ mmHg). Secondary hypertension was excluded in each patient by routine screening investigations (plasma urea, electrolytes, and calcium; urinalysis; ^{131}I Hippuran isotope renography and 24 hour urinary vanillyl mandelic acid excretion). Each patient was an experienced car driver.

A fully ambulatory 24 hour blood pressure recording was obtained from each subject using a transducer perfusion unit,⁷ and a continuous intra arterial blood pressure was recorded on magnetic tape using a miniature cassette recorder (Medilog recorder, Oxford Instruments Ltd). Each recording was begun at approximately 10.00 hours, and before leaving the hospital each patient underwent a graded exercise test on a standard Elema bicycle ergometer. This was a maximal exercise test and involved workloads of 250, 400, 700, and 1000 kpm, each level being continued for four minutes before proceeding to the next grade.

After leaving the hospital each patient returned to his normal work and during the late afternoon (approximately 16.00 hours) drove from his workplace to the hospital. Each patient had a wrist watch, the accuracy of which had previously been checked, and the exact time of the beginning and the end of the driving period were noted on a diary sheet. In the majority of cases the drive was from the centre of London to the periphery and involved moderately heavy city traffic, with no motorway or country driving. As the patients lived in the Harrow area this car journey was similar to that made every day to and from their place of work. On arrival at the hospital, standard pressure calibration signals were recorded on the tape, using a mercury column.

After the initial blood pressure recording each patient was started on antihypertensive treatment with oxprenolol, the dosage of which was adjusted in the clinic to produce satisfactory sphygmomanometric blood pressure control (a diastolic blood pressure less than 95 mmHg). A maximum of 480 mg oxprenolol daily was used and two patients in whom blood pressure control remained poor on that dosage also received a diuretic (cyclopenthiazide 0.5 mg and potassium chloride 1200 mg in a combination tablet). A second 24 hour recording was carried out after an average of 15.8 weeks of treatment. The exercise test was repeated and again the times of the journey made by the patient from his place of work to the hospital in the late afternoon

were noted. The mean daily dosage of oxprenolol used was 331 ± 128 mg and the mean duration of the driving period was 20.9 ± 13.6 minutes before treatment and 15.5 ± 5.1 minutes during treatment.

Analysis of the blood pressure signal recorded on the magnetic tape was performed by a hybrid computer system developed in this department,⁸ which allowed calculation of the mean and variance of systolic and diastolic blood pressure for specified parts of the recording identified accurately on the tape. The same data could also be displayed graphically as an incidence histogram. In addition to analysing the driving period, the mean daytime blood pressure was assessed by computer analysis of the six-hour period from 12.00 to 18.00 hours. This period in the middle of the waking day was used as a measurement of the mean daytime ambulatory blood pressure for each patient. It was a time spent by each patient largely at his place of work engaged in his normal activities.

Blood pressure data were also available from two other sources. Clinic blood pressure, as recorded with a standard sphygmomanometer, was measured after lying supine for five minutes and again after standing for one minute on three occasions before the initial blood pressure recording. Clinic visits were continued during treatment, and the readings made one week before the second intra-arterial recording were regarded as the "treatment" clinic blood pressure. Secondly, the blood pressure response to exercise was recovered from the tape recording using a Medelec fiberoptic recording oscilloscope and the response at 700 kpm/m was measured. This was regarded as moderately severe exercise and was achieved by each of the patients.

This project was approved by the hospital ethical committee.

Results

Data were available from all 15 patients, and in each case pretreatment and treatment observations were compared using a paired Student's *t* test (Table). No side effects were reported by the patients.

(a) BLOOD PRESSURE DURING DRIVING

Inspection of the individual blood pressure traces during the driving period (Fig. 1) indicated that blood pressure was remarkably stable during car driving and that the pressure tended to be higher and more variable during the few minutes immediately before and after the drive, when the patient was walking to, or from, his car. The mean levels of pressure in the untreated patients during driving were similar to mean daytime ambulatory pressure and clinic blood pressure (Table).

Table Blood pressure before and during chronic oxprenolol therapy

	Before treatment	Treatment	Significance
Clinic blood pressure	174.3 (21.5) 112.9 (16.7)	147.0 (14.7) 93.4 (7.8)	$p < 0.001$ $p < 0.001$
Driving blood pressure	176.2 (25.4) 106.7 (12.5)	160.1 (28.2) 92.7 (9.5)	$p < 0.02$ $p < 0.01$
Daytime ambulatory blood pressure	174.3 (21.0) 109.9 (11.1)	150.9 (27.1) 89.1 (14.4)	$p < 0.001$ $p < 0.001$
Blood pressure during bicycle ergometry	225.0 (33.3) 128.0 (15.7)	204.6 (38.8) 110.6 (11.8)	$p < 0.01$ $p < 0.001$

Figures in parentheses indicate standard deviation.

The statistical analysis refers to a paired Student's *t* test.

Treatment reduced mean systolic pressure during car driving in 10 patients and mean diastolic pressure in 12 patients. For the group as a whole the driving blood pressure fell from 176/107 to 160/93 mmHg ($p < 0.02$ and < 0.01 for systolic and diastolic pressure, respectively) during treatment

with oxprenolol (Fig. 2). This corresponded to a reduction of 8.9 per cent for systolic and 12.6 per cent for diastolic pressure. In each case the systolic and diastolic blood pressure variability was investigated by calculating the coefficient of variation, and comparison by a paired *t* test showed no significant change (coefficient of variation before treatment 6.6/7.9 and during treatment 6.7/7.0). Histogram analysis of the blood pressure data from individual patients showed a similar Gaussian distribution before and during treatment (Fig. 3). During the driving period the mean heart rate fell from 99.3 to 81.9 bpm ($p < 0.001$) during treatment with oxprenolol, but there was no effect on heart rate variability (pretreatment pulse interval time coefficient of variation 0.080 and during treatment 0.075, $p > 0.1$). When on treatment patients reported no subjective effects on their driving ability.

(b) AMBULATORY BLOOD PRESSURE

Data were available on the mean daytime blood pressure for each of the patients before and during

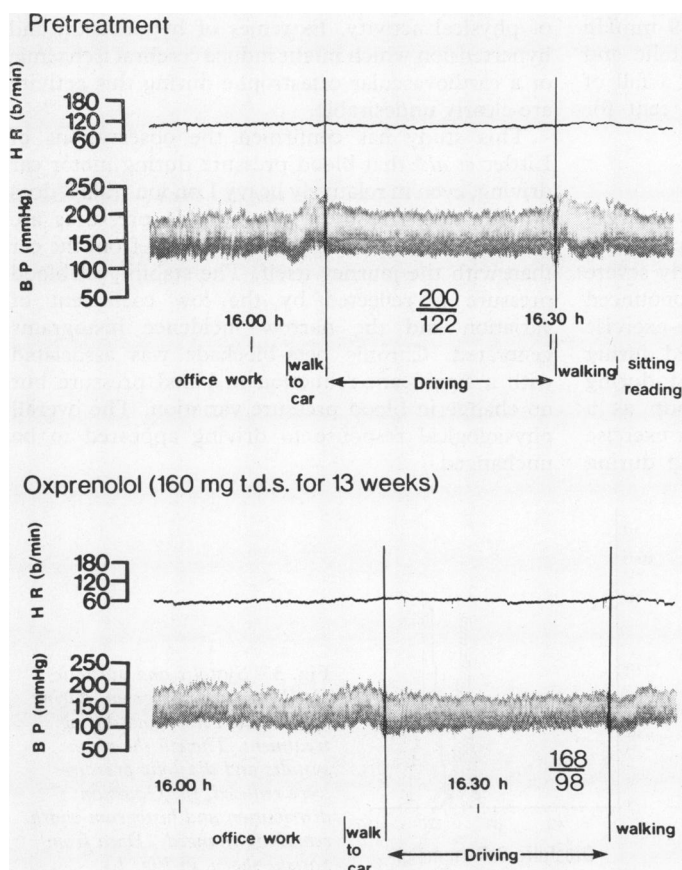


Fig. 1 Blood pressure and heart rate recordings from a single patient during motor car driving. Blood pressure was highest walking to the car and walking from the car at the end of the driving period. During driving, blood pressure remained stable. Though blood pressure is lower during treatment, the blood pressure response is similar.

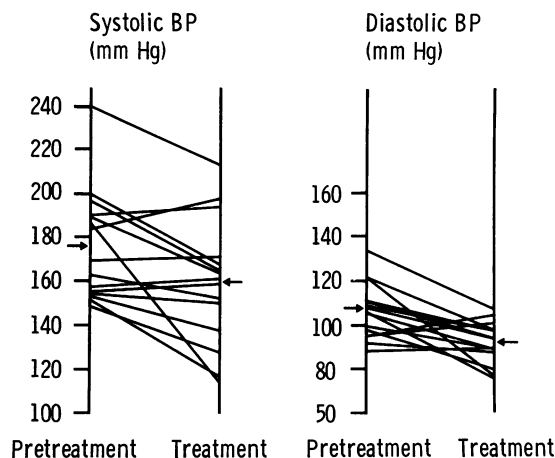


Fig. 2 Mean systolic and diastolic blood pressure in each patient during motor car driving before and during chronic oxprenolol treatment. (The mean for the group is indicated by the arrow.)

treatment. For the group as a whole there was a fall in blood pressure from 174/110 to 151/89 mmHg during treatment ($p < 0.001$ for both systolic and diastolic pressure). This corresponded to a fall of 13.6 per cent for systolic and 18.5 per cent for diastolic pressure.

(c) BICYCLE ERGOMETRY

The highest grade of exercise on the bicycle ergometer that all patients were able to achieve on both occasions was 700 kpm/m. This moderately severe level of work was associated with a pronounced increase in blood pressure from the pre-exercise level in all subjects, and this was measured during the final minute of exercise before and during antihypertensive treatment. For the group as a whole the blood pressure response during exercise changed from 225/128 to 205/111 mmHg during

treatment ($p < 0.01$ and < 0.001 for systolic and diastolic pressure, respectively). This response was reduced in all but three of the 15 patients. The percentage reduction for the group was 9.1 per cent for systolic and 13.3 per cent for diastolic pressure.

(d) CLINIC BLOOD PRESSURE

In all 15 patients treatment was associated with a reduction in clinic systolic and diastolic blood pressures. For the group as a whole the pre-treatment blood pressure fell from 174/113 to 147/93 mmHg ($p < 0.001$ for both systolic and diastolic pressure). This corresponded to a reduction of 14.9 and 16.2 per cent, respectively.

Discussion

In hypertensive subjects, chronic treatment with beta-adrenoceptor blocking agents has been shown to reduce the blood pressure response to dynamic exercise⁹ but to have little effect during isometric exercise¹⁰ and during the "stress" associated with mental arithmetic.¹¹ Driving is a complex activity involving both mental activity and a moderate amount of physical activity. Extremes of hypotension and hypertension which might induce cerebral ischaemia or a cardiovascular catastrophe during this activity are clearly undesirable.

This study has confirmed the observations of Littler *et al.*⁶ that blood pressure during motor car driving, even in relatively heavy London traffic, does not fluctuate greatly. Higher blood pressures are usually associated with the walk to and from the car than with the journey itself. The stability of blood pressure is reflected by the low coefficient of variation and the narrow incidence histograms generated. Chronic beta-blockade was associated with a significant reduction in blood pressure but no change in blood pressure variation. The overall physiological response to driving appeared to be unchanged.

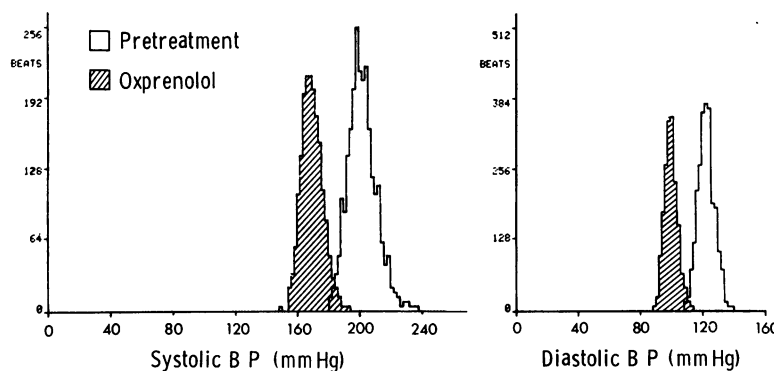


Fig. 3 Systolic and diastolic blood pressure histograms during car driving before and during treatment. Though the mean systolic and diastolic pressures were reduced, the Gaussian distribution and histogram width remain unchanged. (Data from patient shown in Fig. 1.)

Although all 15 patients had a reduced blood pressure during chronic oxprenolol treatment when it was measured in the clinic, only 10 patients had a lower systolic blood pressure while driving. Twelve patients had a lower systolic pressure during bicycle ergometry and 13 had a lower mean daytime systolic blood pressure. The equivalent numbers of patients who had a lower diastolic pressure were 13, 15, and 14 for driving, bicycle ergometry, and mean daytime pressure, respectively. Before treatment the levels of blood pressure recorded during the driving period and the daytime period were similar (176/107 and 174/110 mmHg, respectively). After treatment, however, the blood pressure during driving was not reduced as much as the mean daytime pressure (160/93 and 151/89 mmHg, respectively). This difference between driving and mean daytime pressures was significant for systolic pressure ($p < 0.01$). The percentage reduction produced by treatment was less during the driving period (8.9%/12.6% and 13.6%/18.5% for driving and mean daytime blood pressure, respectively) though this difference failed to reach statistical significance ($p < 0.05$). Blood pressure during exercise was much higher than during driving but the percentage reduction after treatment was similar (9.1%/13.3%) to that observed during car driving.

This suggests that the blood pressure responses during both physical activity and the mental stress associated with driving are only partly a result of beta-adrenergic activity. Taylor *et al.*¹⁰ showed that though hydrochlorothiazide, oxprenolol, bethanidine, methyl dopa, and clonidine all reduced blood pressure at rest, only oxprenolol and bethanidine reduced blood pressure during treadmill exercise and that none of the drugs reduced the increase in blood pressure associated with isometric (handgrip) exercise. Nyberg *et al.*¹¹ found that the increase in blood pressure associated with sustained mental arithmetic was not lessened by either the acute or the chronic administration of alprenolol, propranolol, or metoprolol. Watson *et al.*¹² investigated the effects of chronic beta-adrenergic blockade on ambulatory intra-arterial blood pressure in hospital and found that though both daytime and night-time blood pressures were reduced by treatment, the relative blood pressure reduction during dynamic bicycle ergometry was less than that found during other daytime activities.

An incidental finding in this study was that clinic blood pressure measurements do not always correspond with blood pressure changes in patients exposed to normal environmental stress outside hospital. This is in keeping with other studies using the same or similar recording techniques.¹³⁻¹⁵ We have found that some patients appear to have a good

response to treatment when assessed at rest with the sphygmomanometer, but show no change in the ambulant intra-arterial recording. In a previous report¹⁶ we have suggested that blood pressure measurement during exercise may be more informative than resting clinic blood pressure.

Our study was not controlled in the sense that there was no placebo period and the order of studies was the same in each case. We suspected that placebo and other effects would not affect this type of study which involves large amounts of data, and a double-blind placebo study which we have performed fully supports this view. The study also confirmed the high degree of repeatability of intra-arterial measurements.¹⁷

We conclude that chronic administration of the beta-adrenoceptor blocking agent oxprenolol in hypertensive patients is associated with a reduction in blood pressure during car driving and also in mean daytime blood pressure and in blood pressure during dynamic exercise. There is some evidence that the antihypertensive effect is less during car driving than during other daytime activities (as assessed by the mean daytime blood pressure). The normal blood pressure response to car driving, however, and objective assessment of blood pressure variation are unchanged. These findings support the use of oxprenolol in hypertensive subjects who drive motor vehicles.

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